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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/530,250	04/05/2005	Cameron Black	MC070P	9683

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EXAMINER	
KIFLE, BRUCK	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 08/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/530,250	BLACK, CAMERON	
	Examiner	Art Unit	
	Bruck Kifle, Ph.D.	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *18-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17,22 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *06/30/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Election/Restrictions

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claims 1-17, 22 and 23, drawn to a compound of claim 1, corresponding pharmaceutical composition and use.

Group II, claims 18-21, drawn to complex pharmaceutical compositions and their use.

The inventions listed as Groups I and II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: compounds, corresponding compositions, a method of use and a process of making that are of the same scope are considered to form a single inventive concept under PCT Rule 13.1, 37 CFR 1.475(d). The claims are not so linked as to form a single inventive concept. The complex pharmaceutical compositions and their uses require separate searches and raise different issues of patentability.

During a telephone conversation with Ms. Dianne Brown on July 31, 2006 a provisional election was made with traverse to prosecute the invention of group I, claims 1-17, 22 and 23. Affirmation of this election must be made by applicant in replying to this Office action. Claims 18-21 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claim Rejections - 35 USC § 112

Claims 1-7, 9-17 and 22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification is not adequately enabling for the scope of the compounds claimed.

Applicants have made one compound but have not tested a single compound. This does NOT give a reasonable assurance that all, or substantially all of them, are useful. The claims are not drawn in terms of a recognized genus but are directed to a more or less artificial selection of compounds.

There is no reason why a claim drawn in this way should not be limited to those compounds which are shown to be both new and useful. An Applicant is not entitled to a claim for a large group of compounds merely on the basis of a showing that a selected few are useful and a general suggestion of a similar utility in the others."

Also, see In re Surrey 151 USPQ 724, regarding sufficiency of a disclosure for a Markush group, and MPEP 2164.03 for enablement requirements in cases directed to structure-sensitive arts such as the instant pharmaceutical arts. Note in Surrey, in which testing done on a group of homogeneous compounds having the same core was deemed NOT sufficient to support claims to various hetero groups of a much narrower range than is being claimed herein and located at only one position in the formula. The instant scope is enormous, in the millions of compounds, and therefore one compound within its scope is not remotely representative of such a scope. See MPEP 2164.03.

Claims 1-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

i) The term "heterocyclyl" is indefinite because it is not known how many atoms make up the ring, which atoms are present and what kind of a ring (monocyclic, bicyclic, spiro, fused, bridged, saturated, etc.) is intended. See the rings formed by R^3 and R^4 and R^4 and R^8 where the number and kind of heteroatoms present within the rings formed is not known.

ii) The term "heteroaryl" is indefinite because it is not known how many atoms are present, how many and what kind of heteroatoms are involved, what size ring is intended and how many rings are present.

iii)In page 39, line 11, it is not clear what the phrase "said groups" refers to. Appropriate clarification is required.

iv) The last line of claim 1 reads "and the pharmaceutically acceptable salts, stereoisomers and N-oxide derivatives thereof." This is not proper Markush language. It is suggested to rewrite this as, for example, "or a pharmaceutically acceptable salt, stereoisomer or and N-oxide thereof." The term "derivative" is undeterminable and deletion is suggested.

v) Claim 13 depends on itself. Correction is required.

Claim 10 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 9 and claim 22 is objected to as being a substantial duplicate of claims 1-8. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other

as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Claim 10 is a product-by-process claim. Regarding claim 22, the intended use does not have patentability weight.

Claim 23 provides for the use of a compound, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 23 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claims 12-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for inhibiting cathepsin activity, treating or preventing a disease selected from: osteoporosis, glucocorticoid induced osteoporosis, Paget's disease, abnormally increased bone turnover, periodontal disease, tooth loss, bone fractures, rheumatoid arthritis, osteoarthritis, periprosthetic osteolysis, osteogenesis imperfecta, metastic bone disease, hypercalcemia of malignancy or multiple myeloma, treating or preventing bone loss and treating cathepsin dependent conditions in a mammal.

Claims 12, 13 and 17 read on treating a disease or condition, which has not been specified. The how to use portion of the statute has not been addressed. This means that Applicants must teach the skilled practitioner, in this case a physician, how to treat a given subject. The physician clearly must know what diseases and what symptoms are to be treated.

Is extensive experimentation required on the part of a potential infringer to determine if his use of Applicants' compounds falls within the limitations of applicants' claim? *In re Kirk and Petrow*, 153 USPQ 48 (CCPA 1967). As the Supreme Court said in *Brenner v. Manson*, 148 USPQ at 696: "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." As U.S. Court of Customs and Patent Appeals stated *In re Diedrich* 138 USPQ at 130, quoting with approval from the decision of the board: "We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound in terms of possible use so general as to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates."

In this case, Applicants have not provided what is being treated by claims 12, 13 and 17 who the subject in need is, how one can identify said subject (i.e. how one can identify a subject in need), given no specific dose, given no specific dosing regimen, given no specific route of administration, and do not specify what diseases or symptom they intend to treat.

Regarding claims 14-16, Applicants have not demonstrated nor have they alleged there is any correlation between the *in vitro* assays they disclose in pages 30-32 and clinical efficacy against any disease. Case law is clear on this point. In an unpredictable art, such as physiological activity and disease therapy, *in vitro* assays may be used for enablement only if there is a well-established correlation between the assay and clinical efficacy.

The how to use requirement of the enablement statute, when applied to method claim, refers to operability and how to make the claimed method work "The factors to be considered (in making an enablement rejection) have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims", In re Rainer 146 USPQ 218 (1965); In re Colianni, 195 USPQ 150, Ex parte Formal, 230 USPQ 546. The issue is the correlation between clinical efficacy for the disease in claims 14-16 and Applicants' *in vitro* Cathepsin assay.

a) Determining if any particular claimed compound would prevent or treat any of the diseases would require synthesis of the compound, formulation into a suitable dosage form, and subjecting it to clinical trials with a number of fundamentally different diseases listed above, or to testing them in an assay known to be correlated to clinical efficacy of such treatment. This is a large degree of experimentation.

b) The direction concerning treating these diseases found in the specification merely states Applicants' intention to do so. How is the skilled physician to know what dose to use for each of these different diseases? The assays described in the specification have no data.

Applicants do no assert and it is not art-recognized that these *in vitro* assays are correlated to clinical efficacy of the diseases objected to.

c) There is no working example of treatment of any rejected disease in man or animals.

d) The nature of the invention is clinical treatment and prevention of diseases with inhibitors of cathepsin activity, which involves physiological activity.

e) The state of the clinical arts in inhibitors of cathepsin activity related diseases is extensive with no single report of success.

f) The artisan using Applicants invention would be a physician with a MD degree and several years of experience.

g) It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See In re Fisher, 427 F.2d 833, 839, 166 USPQ l8, 24 (CCPA 1970).

h) The scope of the claims involves all of the thousands of compounds as well as the treatment and prevention of diseases embraced by the claims. Thus, the scope of the claim is very broad. The scope of uses embraced by these claims is not remotely enabled based solely on instant compounds ability to inhibit cathepsin activity.

MPEP 2164.0l(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here and undue experimentation will be required to practice Applicants' invention.

Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. Tossing out the mere germ of an idea does not constitute enabling disclosure. Genentech Inc. v. Novo Nordisk 42 USPQ2d 1001.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

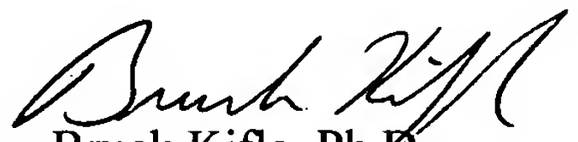
Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Marquis et al. (WO 00/38687). The claims read on the compounds of RN 281214-87-7P, 281214-94-6P, 281214-95-7P and 281214-99-1P of the reference. See CAS abstract provided for Applicants convenience. These compounds are also disclosed on WO 01/95911.

The reference also teaches compounds of RN281216-56-6P and 281218-62-0P which are compounds wherein R^4 and R^8 together form a ring. See CAS abstract.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruck Kifle, Ph.D. whose telephone number is 571-272-0668. The examiner can normally be reached Mondays to Fridays between 8:30 AM and 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Bruck Kifle, Ph.D.
Primary Examiner
Art Unit 1624

BK
July 31, 2006